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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/816,591	04/01/2004	Laura Fuertes-Lopez	FUERTES-LOPEZ	8510

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/816,591	FUERTES-LOPEZ ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/9/07 has been entered. Applicant's amendment and response also received on 8/9/07 have been entered. Claims 1-23 are now canceled and new claim 24 has been added. Claims 24 is currently pending in the instant application.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Interview Summary

Applicant's record of the interview between the applicant's representative, Dr. O.M. Zaghmout and the examiner of record which took place on 7/19/07 states that the examiner agreed that introduction of the limitation of claim 23 into claim 22 would render the claim free of the prior art. This is not completely accurate. The examiner in fact noted that the 103 rejection of record at the time of the interview was correctly applied to both claims 22 and 23. The examiner

pointed out that claim 23 recites that the oligopeptide "comprises" SEQ ID NO:3, and suggested that inclusion of the closed language "consisting of" might overcome the rejection of record. It is further noted that the examiner indicated that the inclusion of additional limitations to the claims would required additional search and consideration.

Priority

The previous office action acknowledged applicant's claim for foreign priority based on applications filed in Germany on October 2, 2001 or November 12, 2001, but noted that while , the applicant has provided a certified copy of DE 101 56 679.4 in German, the office has only received a single cover page for DE 101 48 732.0, which does not constitute a certified copy. As indicated in the previous office action, a complete certified copy of DE 101 48 732.0 is required to fully comply with 35 U.S.C. 119(b).

The applicant has not addressed this issue or provided a complete certified copy of DE 101 48 732.0 with the response filed on 8/9/07.

Double Patenting

The provisional rejection of previously pending claims 22-23 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over previously pending claims 29-31 of copending Application No. 10/816,465, hereafter referred to as the '465 application, is withdrawn over canceled claims 22-23. The provisional rejection has not been

applied to new claim 24 as the '465 application has been amended such that the only pending claim, claim 41, is a method claim, not a product claim.

Claim Rejections - 35 USC § 103

The rejection of claims 22-23 under 35 U.S.C. 103(a) as being unpatentable over Gurunathan et al. (1997) J. Exp. Med., Vol. 186(7), 1137-1147, in view of U.S. Patent No. 6,451,593 (2002), hereafter referred to as Wittig et al., is withdrawn in view of the cancellation of claims 22-23. It is further noted that the rejection has not been applied to new claim 24 because new claim 24 recites that the vaccine comprises an oligopeptide consisting of the amino acid sequence of SEQ ID NO 3. Although Wittig et al. teach the covalent attachment of the nuclear localization sequence (NLS) from SV40, a sequence which inherently comprises PKKKRKV (SEQ ID NO: 3), to a construct as claimed, Wittig et al. does not specifically teach covalently attaching an oligopeptide consisting of SEQ ID NO 3.

Applicant's amendment has necessitated the following new grounds of rejection.

Claim 24 is newly rejected under 35 U.S.C. 103(a) as being unpatentable over Gurunathan et al. (1997) J. Exp. Med., Vol. 186(7), 1137-1147, in view of U.S. Patent No. 6,451,593 (2002), hereafter referred to as Wittig et al., and Makkerh et al. (1996) Current Biology, Vol. 6 (8), 1025-1027.

The applicant claims a vaccine for vaccinating against leishmania comprising a DNA expression construct comprising a covalently closed linear DNA molecule comprising a linear double stranded region comprising a coding sequence under control of a promoter, where the single strands forming the double strand are linked a short single stranded loops of DNA, and where the construct is covalently linked to an oligopeptide, wherein the construct encodes a p36 LACK leishmania antigen, and wherein the oligopeptide consists of PKKKRKV (SEQ ID NO:3).

Gurunathan et al. teaches a DNA expression construct encoding the p36 LACK antigen from *Leishmania major* operatively linked to the CMV promoter and a polyA sequence and the use of the construct as a vaccine to generate protective immunity against *Leishmania major* in a mammal (Gurunathan et al., pages 1137-1139).

Gurunathan et al. differs from the instant invention in that the DNA expression construct is plasmid and in that the DNA is not covalently linked to an oligopeptide such as PKKKRKV. Wittig et al. supplements Gurunathan et al. by teaching dumbbell shaped DNA expression constructs comprising covalently closed linear DNA that contains only a coding sequence operably linked to a promoter and polyA termination sequence where the linear ends are linked by short single stranded loops of DNA, and wherein the construct is further covalently linked to a peptide which directs transport of the construct across a cell's endosome or into the nucleus (Wittig et al., claims 1-11, and columns 5-8)). In particular, Wittig et al. specifically teaches the use of the nuclear localization sequence (NLS) from SV40, a sequence which inherently comprises PKKKRKV (Wittig et al., column 5). Wittig et al. also teaches a vaccine comprising this construct for treating infectious diseases (Wittig et al., columns 1 and 8). Wittig et al. further

provides motivation for using a dumbbell DNA expression construct linked to a peptide over a plasmid DNA expression construct. Wittig et al. teaches that because the dumbbell construct consists only of a promoter-gene-terminator sequence, these constructs have none of the disadvantages of plasmid constructs, which include their size, which inhibits fast transport into the cell's nucleus, and the presence of unwanted background sequences, including bacterial sequences, which can lead to unintended immune responses (Wittig et al., columns 2-3, bridging paragraph).

While Wittig et al. does teach to use an oligopeptide covalently attached to the DNA construct for nuclear transport, and teaches the use of the NLS from SV40, Wittig et al. does not specifically teach that the peptide consists of PKKKRKV. However, at the time of filing, the exact nuclear localization sequence (NLS) of SV40 was known. Makkerh et al. teaches that the sequence consisting of PKKKRKV is the defined nuclear localization sequence of SV40, which can be used to target heterologous molecules to the nucleus (Makkerh et al., page 1025, and Table I, page 1027).

Therefore, based on the advantages to using dumbbell DNA expression constructs over plasmid constructs for immunization as taught by Wittig et al., the motivation to covalently attach a peptide such as an NLS from SV40 also provided by Wittig et al., and the known sequence of the NLS peptide from SV40 as provided by Makkerh et al., it would have been *prima facie* obvious to the skilled artisan at the time of filing to use a dumbbell DNA construct encoding p36 LACK linked to the defined NLS peptide PKKKRKV of Makkerh et al. according to the teachings of Wittig instead of a plasmid construct in the methods of immunizing against Leishmania taught by Gurunathan et al. Further, based on the substantial guidance for making

dumbbell constructs provided by Wittig et al., the skilled artisan would have had a reasonable expectation of success in making a dumbbell DNA expression construct encoding the p36 LACK antigen covalently linked to a peptide such as the NLS PKKKRKV peptide from SV40.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 24 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 recites in lines 14-15 that the DNA construct is covalently linked to at least one oligopeptide to increase transfection efficacy. The claim in lines 18-20 then recites, "..wherein the vaccine further comprises at least one oligopeptide consisting of the amino acid sequence of SEQ ID 3". It is unclear whether the oligopeptide consisting of the amino acid sequence of SEQ ID 3 is the same as the oligopeptide covalently linked to the DNA construct, or whether the applicant intends there to be one oligopeptide covalently linked to the DNA construct and an additional oligopeptide consisting of SEQ ID NO 3 which is present in the vaccine composition which may or may not be associated covalently or otherwise to the DNA construct present in the vaccine. As such, the metes and bounds of the claim cannot be determined

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 24 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claim 24 recites a vaccine composition comprising a DNA construct covalently linked to at least one oligopeptide, "..wherein the vaccine further comprises at least one oligopeptide consisting of the amino acid sequence of SEQ ID 3". As noted in the rejection of the claim above under 35 U.S.C. 112, second paragraph, it is unclear whether the claim is intended to encompass a vaccine wherein the covalently linked oligo consists of the sequence of SEQ ID 3, or a vaccine in which an oligo is covalently linked to the construct and which further includes an oligo of SEQ ID 3 which may or may not be covalently linked to the DNA construct. If the second embodiment is the subject matter intended to be encompassed by the claim, then the specification does not provide the requisite written description of such a vaccine in which a second oligo is present in the vaccine without being covalently linked to the DNA construct. The disclosure in the instant specification is limited to a discussion of covalently linking an oligopeptide comprising or consisting of a nuclear localization sequence to a DNA expression construct to increase transfection and does not teach or suggest the inclusion of non-covalently linked oligos of any sequence in the vaccine compositions. It is further noted that the applicant has not pointed to any particular page, paragraph, or line in the specification which provides

support for this new limitation. The applicant states that claim 24 is based on previously pending claims 22 and 23. However, the previous claims, and in particular claim 23, identified the oligo comprising SEQ ID 3 as being the oligo which is covalently linked to the DNA construct. Therefore, neither the previously pending claims nor the specification supports the scope of vaccine now claimed in which a second oligo of SEQ ID 3 is present in the vaccine and is not covalently linked to the DNA construct. Therefore, the limitation in new claim 24 which recites, "..:wherein the vaccine further comprises at least one oligopeptide consisting of the amino acid sequence of SEQ ID 3" constitutes new matter.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633